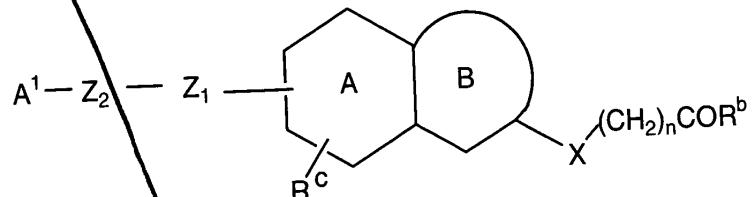


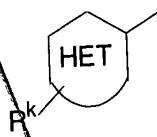
What is claimed is:

1. A compound of the formula I



wherein

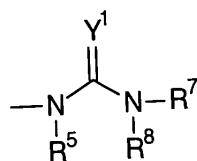
10 A<sup>1</sup> is a 5-9 membered monocyclic or 7-12 membered polycyclic heterocycle of the formula



15 containing at least one nitrogen atom and 0 to 5 heteroatoms or groups selected from O, N, S, SO<sub>2</sub> or CO; optionally saturated or unsaturated; optionally substituted by one or more R<sup>k</sup> selected from the group consisting of hydroxy, alkyl, alkoxy, alkoxy-alkyl, thioalkyl, haloalkyl, cyano, amino, alkylamino, halogen, acylamino, sulfonamide and -COR wherein R is hydroxy, alkoxy, alkyl or amino;

20

or A<sup>1</sup> is



25 wherein Y<sup>1</sup> is selected from the group consisting of N-R<sup>2</sup>, O, and S;

*A<sup>1</sup>  
cont*

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5        R<sup>2</sup> is selected from the group consisting of H; alkyl; aryl; hydroxy; alkoxy; cyano; alkenyl; alkynyl; amido; alkylcarbonyl; arylcarbonyl; alkoxy carbonyl; aryloxycarbonyl; haloalkylcarbonyl; haloalkoxy carbonyl; alkylthiocarbonyl; arylthiocarbonyl; acyloxymethoxy carbonyl;

10      R<sup>2</sup> taken together with R<sup>7</sup> forms a 4-12 membered dinitrogen containing heterocycle optionally substituted with one or more substituent selected from the group consisting of lower alkyl, thioalkyl, alkylamino, hydroxy, keto, alkoxy, halo, phenyl, amino, carboxyl or carboxyl ester, and fused phenyl;

15      or     R<sup>2</sup> taken together with R<sup>7</sup> forms a 4-12 membered heterocycle containing one or more heteroatom selected from O, N and S optionally unsaturated;

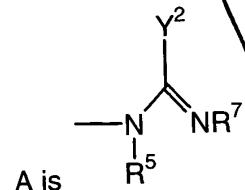
20      or     R<sup>2</sup> taken together with R<sup>7</sup> forms a 5 membered heteroaromatic ring fused with a aryl or heteroaryl ring;

25      20      R<sup>7</sup> (when not taken together with R<sup>2</sup>) and R<sup>8</sup> are independently selected from the group consisting of H; alkyl; alkenyl; alkynyl; aralkyl; amino; alkylamino; hydroxy; alkoxy; arylamino; amido, alkylcarbonyl, arylcarbonyl; alkoxy carbonyl; aryloxy; aryloxycarbonyl; haloalkylcarbonyl; haloalkoxycarbonyl; alkylthiocarbonyl; arylthiocarbonyl; acyloxymethoxycarbonyl; cycloalkyl; bicycloalkyl; aryl; acyl; benzoyl;

30      or     NR<sup>7</sup> and R<sup>8</sup> taken together form a 4-12 membered mononitrogen containing monocyclic or bicyclic ring optionally substituted with one or more substituent selected from lower alkyl, carboxyl derivatives, aryl or hydroxy and wherein said ring contains 0-1 heteroatom, selected from the group consisting of O, N and S;

$R^5$  is selected from the group consisting of H, and alkyl;

or



*a'*  
*Cont*

5

wherein  $Y^2$  is selected from the group consisting of alkyl; cycloalkyl; bicycloalkyl; aryl; monocyclic heterocycles;

10

$Z_1$  is selected from the group consisting of  $CH_2$ , O,  $CH_2O$ , NH, CO, S, SO,  $CH(OH)$  and  $SO_2$ ;

15

$Z_2$  is a 1-5 carbon linker optionally containing one or more heteroatom selected from the group consisting of O, S and N; alternatively  $Z_1 - Z_2$  may further contain a carboxamide, sulfone, sulfonamide, alkenyl, alkynyl, or acyl group; wherein the carbon and nitrogen atoms of  $Z_1 - Z_2$  are optionally substituted by alkyl, alkoxy, thioalkyl, alkylsulfone, aryl, alkoxyalkyl, alkylamino, heteroaryl, hydroxy, alkenyl, alkynyl, carboxyalkyl, halogen, haloalkyl or acylamino;

20

is an integer 0, 1 or 2;

25

$R^c$  is selected from the group consisting of hydrogen, alkyl; halogen, hydroxy, nitro, alkoxy, amino, haloalkyl, aryl, heteroaryl, alkoxyalkyl, aminoalkyl, hydroxyalkyl, thioalkyl, alkylamino, arylamino, alkylsulfonylamino, acyl, acylamino, sulfonyl, sulfonamide, allyl, alkenyl, methylenedioxy, ethylenedioxy, alkynyl, alkynylalkyl, carboxy, alkoxy carbonyl, carboxamido, cyano, and  $-(CH_2)_n-COR$  wherein  $n$  is 0-2 and  $R$  is selected from hydroxy, alkoxy, alkyl and amino;

30

X is selected from the group consisting of -O-, CO, SO<sub>2</sub>, NR<sup>m</sup> and (CHR<sup>p</sup>)<sub>n</sub>; wherein R<sup>p</sup> and R<sup>m</sup> are H or alkyl, n is 0-2;

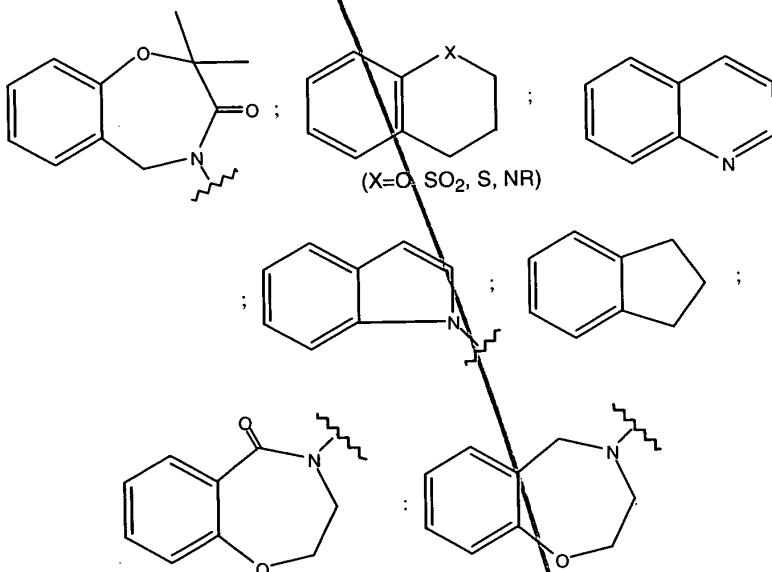
5

$R^b$  is  $X_3 - R^h$  wherein  $X_3$  is selected from the group consisting of O, S and  $NR^i$  wherein  $R^h$  and  $R^i$  are independently selected from the group consisting of H, alkyl, acyl, aryl, aralkyl and alkoxyalkyl; and

10

The ring A-B ,  
consisting of

is selected from the group



15

all optionally substituted and bonded to X and Z<sub>1</sub> at any position;

and pharmaceutically acceptable salts, isomers, enantiomers, tautomers, racemates and polymorphs thereof.

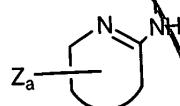


is selected

2. A compound according to Claim 1 wherein  $R^k$

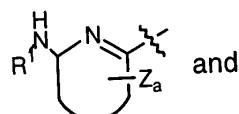
from the group consisting of

*A<sup>1</sup>  
Cont*

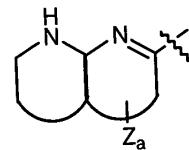


5

B2



B3



B4

wherein  $Z_a$  is H, alkyl, alkoxy, hydroxy, amine, alkylamine, dialkylamine, carboxyl, alkoxy carbonyl, hydroxyalkyl, halogen or haloalkyl and  $R^1$  is H, alkyl, alkoxyalkyl, acyl, haloalkyl or alkoxy carbonyl, and pharmaceutically acceptable salts, isomers, enantiomers, tautomers, racemates and polymorphs thereof.

10

15

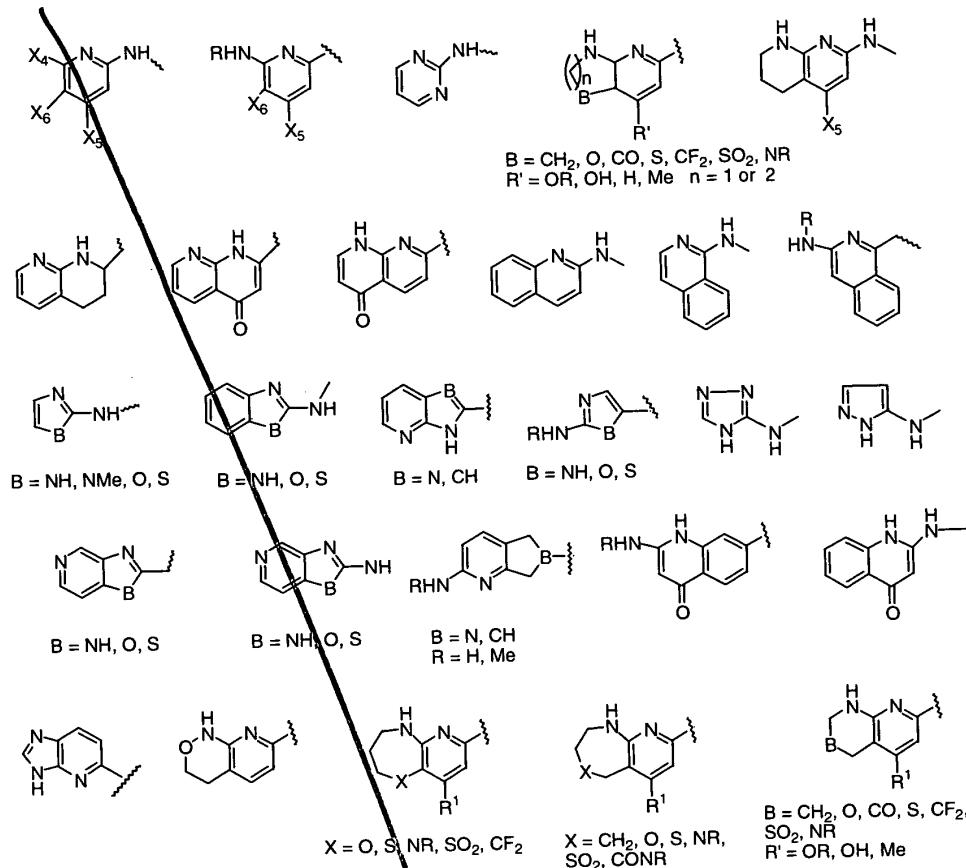


is selected

3. A compound according to claim 1 wherein  $R^k$

from the group consisting of

$a'$   
cont



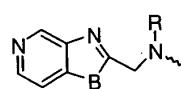
wherein  $X_4$  and  $X_5$  are selected from the group consisting of H, alkyl, branched alkyl, alkylamino, alkoxyalkylamino, haloalkyl, thioalkyl, halogen, amino, alkoxy, aryloxy, alkoxyalkyl, hydroxy, cyano, acylaminomethyl, methoxy, amine, methylamine, trifluoromethyl, dimethyl-amine, hydroxy, chloro, bromo, fluoro and cyano;  $X_6$  is H, alkyl, hydroxy, halogen, alkoxy and haloalkyl; the pyridyl ring can be fused with a 4 - 8 membered ring, optionally saturated or unsaturated, and pharmaceutically acceptable salts, isomers, enantiomers, tautomers, racemates and polymorphs thereof.

15 4. A compound according to claim 1 wherein when  $Z_1$  is CO or  $\text{SO}_2$ , and the linkage  $A^1-Z_2$  is a heterocycle derived ring system selected from the group consisting of pyridine, imidazole, thiazole, oxazole, benzimidazole, and imidazopyridine, and pharmaceutically

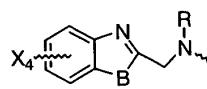
acceptable salts, isomers, enantiomers, tautomers, racemates and polymorphs thereof.

5. A compound according to claim 4 wherein the heterocycle derived ring systems for A<sup>1</sup>-Z<sub>2</sub> are selected from the group consisting of:

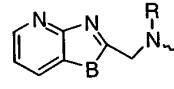
*a' Chem*



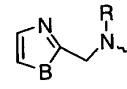
B = NH, O, S  
R = H, Me



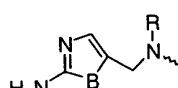
B = NH, O, S  
R = H, Me



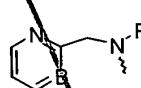
B = NH, O, S  
R = H, Me



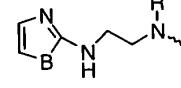
B = NH, O, S  
R = H, Me



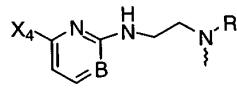
B = NH, O, S  
R = H, Me



B = N, CH  
R = H, Me



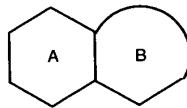
B = NH, O, S  
R = H, Me



B = N, CH  
R = H, Me

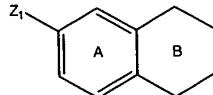
10 and pharmaceutically acceptable salts, isomers, enantiomers, tautomers, racemates and polymorphs thereof.

6. A compound according to Claim 1 wherein the ring A-B



is a tetrahydronaphthalene

15

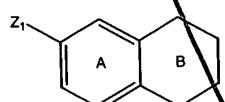


and Z<sub>1</sub> is S, and pharmaceutically acceptable salts, isomers, enantiomers, tautomers, racemates and polymorphs thereof.

7. A compound according to claim 1, wherein the ring A-B



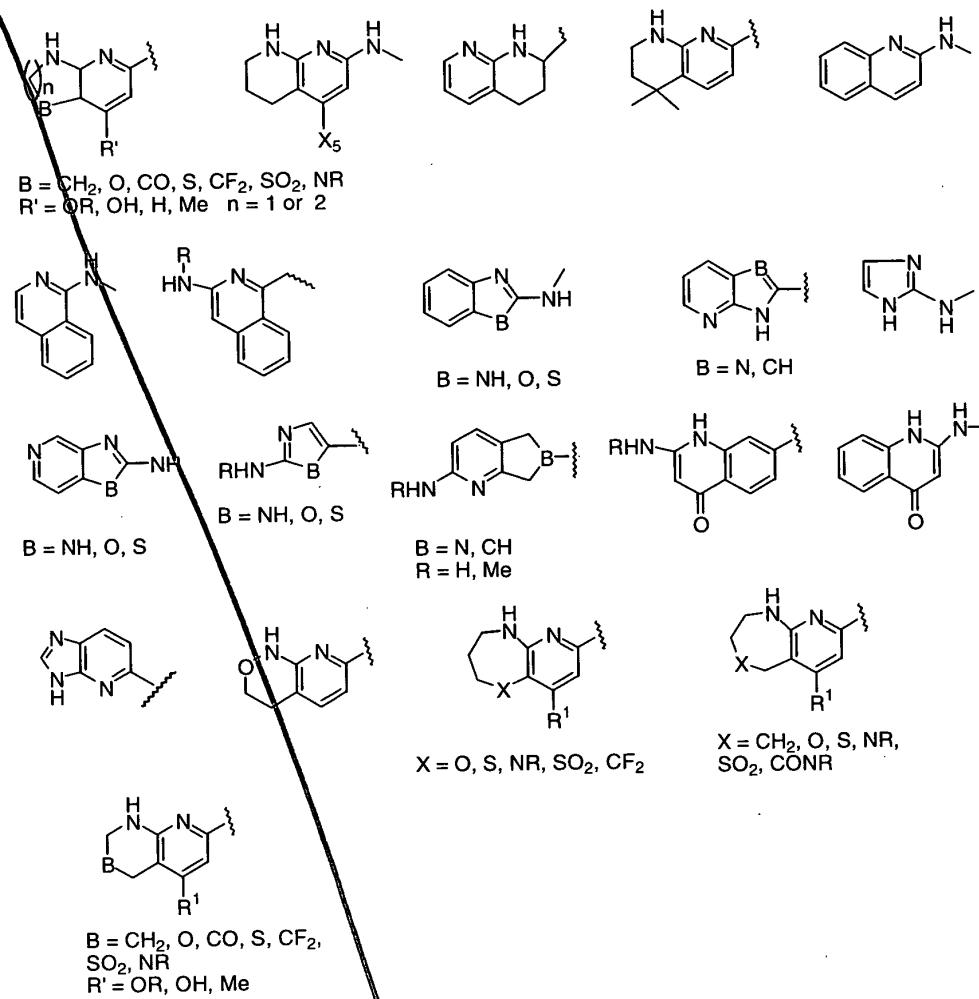
is a tetrahydronaphthalene



5 Z<sub>1</sub> is a CH<sub>2</sub>;

10 A<sup>1</sup> is selected from the group consisting of:

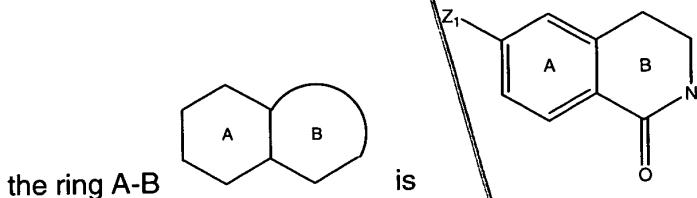
A  
B  
C  
D  
E  
F  
G  
H  
I  
J  
K  
L  
M  
N  
O  
P  
Q  
R  
S  
T  
U  
V  
W  
X  
Y  
Z



and pharmaceutically acceptable salts, isomers, enantiomers, tautomers, racemates and polymorphs thereof.

5

8. A compound according to claim 1, wherein

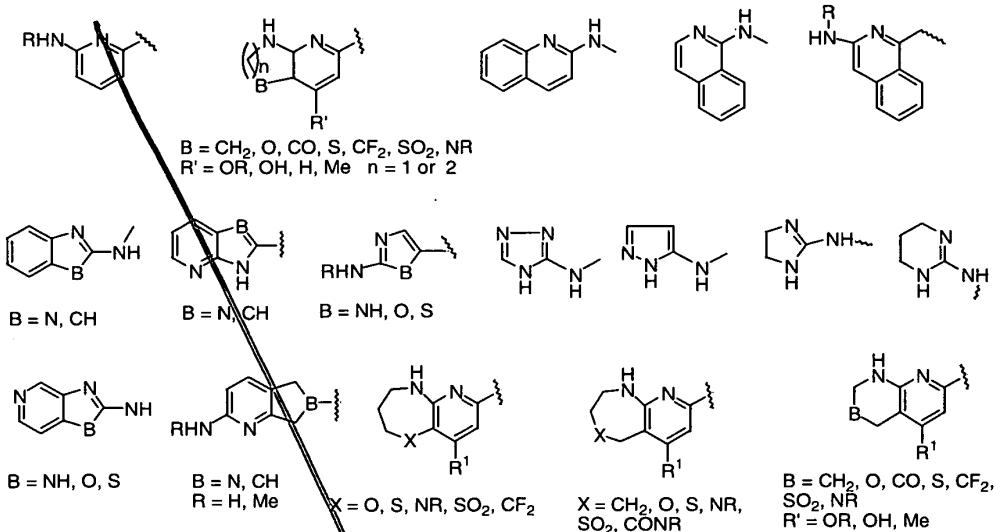


the ring A-B

is

$A^1$  is selected from the group consisting of :

10



and pharmaceutically acceptable salts, isomers, enantiomers, tautomers, racemates and polymorphs thereof.

5 9. A compound according to claim 1 selected from the group consisting of:  
[2,2-dimethyl-3-oxo-8-[3-(pyridin-2-ylamino)propoxy]-2,3-dihydro-1,4-benzoxazepin-4(5H)-yl]acetic acid;

10 1,2,3,4-tetrahydro-6-[3-(2-pyridinylamino)propoxy]-2-isoquinoline-propanoic acid;

{5-[3-(pyridin-2-ylamino)propoxy]-1H-indol-1-yl}acetic acid;

2,3-dihydro-5-[3-(2-pyridinylamino)propoxy]-1H-indene-2-acetic acid;

2, 3, 4, 5-tetrahydro-5-oxo-8-[3-(2-pyridinylamino)propoxy]-1,4-benzoxazepine-4-acetic acid;

15 2,3,4,5-tetrahydro-8-[3-(2-pyridinylamino)propoxy]1,4-benzoazepine-4-acetic acid;

1,2,3,4-tetrahydro-1-oxo-6-[3-(2-tetrahydropyrimidinyl)amino]-propoxy]-2-isoquinolineacetic acid;

20 3,4-dihydro-7-[3-(2-pyridinylamino)propoxy]-2H-1-benzopyran-3-acetic acid;

(6-{[3-(pyridin-2-ylamino)propyl]thio}-1,2,3,4-tetrahydronaphthalen-2-yl)acetic acid;

*Off*  
*Off*  
*C/*  
*cont*

1,2,3,4-tetrahydro-6-[2-(5,6,7,8-tetrahydro-1,8-naphthyridyl)-aminoethoxy]2-naphthaleneacetic acid, and pharmaceutically acceptable salts, isomers, enantiomers, tautomers, racemates and polymorphs thereof.

5 10. A pharmaceutical composition comprising a therapeutically effective amount of a compound of Claims 1-9 and a pharmaceutically acceptable carrier.

10 11. A method for treating conditions mediated by the  $\alpha_v\beta_3$  integrin in a mammal in need of such treatment comprising administering an effective  $\alpha_v\beta_3$  inhibiting amount of a compound of Claims 1-9.

15 12. The method according to Claim 11 wherein the condition treated is selected from the group consisting of tumor metastasis, tumor growth, solid tumor growth, angiogenesis, osteoporosis, humoral hypercalcemia of malignancy, smooth muscle cell migration, restenosis, atherosclerosis, macular degeneration, retinopathy, and arthritis.

20 13. A method for treating conditions mediated by the  $\alpha_v\beta_5$  integrin in a mammal in need of such treatment comprising administering an effective  $\alpha_v\beta_5$  inhibiting amount of a compound of Claims 1-9.

25 14. The method according to Claim 13 wherein the condition treated is selected from the group consisting of tumor metastasis, tumor growth, solid tumor growth, angiogenesis, osteoporosis, humoral hypercalcemia of malignancy, smooth muscle cell migration, restenosis, atherosclerosis, macular degeneration, retinopathy, and arthritis.

30 15. A method of treating neoplasia in a patient in need thereof comprising administering a compound of Claims 1-9 in combination with a chemotherapeutic agent.

cont

16. A compound of Claims 1-9 that selectively antagonizes the  $\alpha_v\beta_3$  and the  $\alpha_v\beta_5$  integrins, over the  $\alpha_v\beta_6$  integrin.

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